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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of R. WENGER et al. .

Serial No.: 09/720,923

Filed: December 28, 2000

Assigned to: DEBIOPHARM S.A.

FOR: NOVEL CYCLOPORIN HAVING AN IMPROVED ACTIVITY
PROFILE.

INFORMATION DISCLOSURE STATEMENT

To the Honorable Commissioner of Patents and Trademarks
Washington, D.C.

Sir :

In accordance with the duty of disclosure set forth in 37 C.F.R. § 1.56 and pursuant to 37 C.F.R. 1.97-1.99 the Applicant hereby submits:

(a) a list of prior art referred to by the Applicant in the specification of the application and/or which has been cited in the Search Report prepared by the European Patent Office (EPO) in respect of the corresponding International Patent Application No.PCT/IB99/01232;

(b) a copy of this Search Report attached in order to inform the U.S. Examiner of the first opinion of the Examiner of the EPO, and those portions of the references found pertinent by the latter;

(c) a copy of the references cited under (a) namely:

- US 4 108 985 A,

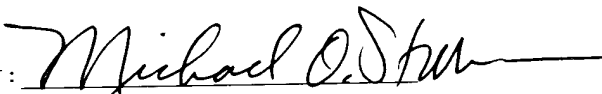
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SEARCHED 17 84

- US 4 220 641 A,
- US 4 288 431 A,
- US 4 554 351 A,
- US 4 396 542 A,
- US 4 814 323 A,
- US 4 210 581 A,
- EP 0 034 567 B,
- EP 0 194 972 B,
- EP 0 484 281 B
- WO 86 02080,
- US 4 441 644 in lieu of EP 0 054 782,
- US 5 948 884 in lieu of WO 97 04005,
- R. Wenger, Synthesis of Cyclosporine and Analogues :
Structure, Activity, Relationships, of New
Cyclosporine Derivatives, Transplantation Proceedings,
Vol. 15, Suppl. 1, pp 2230-2241, 1983,
- R. Wenger, Synthesis of Cyclosporine and Analogues :
Structural Requirements for Immunosuppressive
activity, Angewandte Chemie, International Ed. in
English, Vol. 24, n°2, pp. 77-85, 1985,
- R. Wenger, Cyclosporine and Analogues - Isolation and
Synthesis - Mechanism of Action and Structural
Requirements for Pharmacological Activity, Progress in
the Chemistry of Organic natural products, Vol. 50,
pp. 123-137, 1986,

- S. O'Keefe et al., FK-506- and CsA- sensitive activation of the interleukin-2 promoter by calcineurin, *Nature*, Vol. 357, pp 692-694, 1992,
- E.K. Franke et al., Cyclophilin Binding to the Human Immunodeficiency Virus Type 1 Gag Polyprotein Is Mimicked by an Anti-Cyclosporine Antibody, *Journal of Virology*, Vol. 69, n°9, Sept. 1995,
- E.K. Franke et al., Specific Incorporation of Cyclophilin A into HIV-1 virions, *Nature*, Vol. 372, pp 359-362, 1994,
- C. Papageorgiou et al., Anti HIV-1 Activity of a Hydrophilic Cyclosporin Derivative with Improved Binding Affinity to Cyclophilin A, *Bioorganic & Medicinal Chemistry Letters*, Vol. 6, n° 1, pp 23-26, 1996,
- R. Wenger, Synthesis of Cyclosporine, *Helvetica Chimica Acta*, Vol. 67, Fasc. 2, pp 502-525, 1984,
- M. Cebrat et al. Immunosuppressive Activity of Hymenistatin I, *Peptides*, Vol. 17, n° 2, pp 191-196, 1996,
- V. Quesniaux et al., Cyclophilin binds to the Region of Cyclosporine Involved in its Immunosuppressive Activity, *European Journal of Immunology*, n° 17, pp 1359-1365, 1987,
- T. Meo, the MLR Test in the Mouse, *Immunological Methods*, Eds, Académie Press., pp 227-239, 1979,
- Kobel et al., Directed Biosynthesis of Cyclosporine, *European Journal of applied Microbiology and biotechnology* 14, pp 237-240, 1982, and

- Wenger et al. Cyclosporine Chemistry, Structure-activity relationships and mode of action, progress in Clinical Biochemistry and Medecine, Vol 2, pp 176, 1986.

Respectfully submitted,

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